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INTRODUCTION:

The purpose of the research supported by this award is to conduct a Phase II clinical trial (study) of an adenovirus/PSA (Ad/PSA) vaccine for the treatment of prostate cancer. Two protocols will be used in the trial: #1 - *Phase II study of Adenovirus/PSA vaccine in men with recurrent prostate cancer after local therapy*; and #2 - *Phase II study of Adenovirus/PSA vaccine in men with hormone refractory prostate cancer*. In the first protocol men with newly recurrent prostate cancer will be randomized to one of two arms of the study. Patients in Arm A will receive the Ad/PSA vaccine only; three injections spaced 30 days apart. Patients in Arm B will receive androgen deprivation therapy (ADT) followed at day 14 by the Ad/PSA vaccine, again with three injections. In the second protocol men with hormone refractory prostate cancer will be injected with the vaccine only, three injections 30 days apart. The patients will be followed for toxicity, the development of anti-PSA immune responses, and evidence of a clinical effect of the vaccination. The latter includes changes in serum PSA levels and in the PSA doubling times (PSADT). Patients in protocol #2 will also have CT and bone scans to monitor their prostate cancer.

BODY:

Following an initial meeting with representatives of the DOD's PCRP, including the Human Subjects Research Review Board (HSRRB) on December 12, 2006, we spent 13 months revising our protocols and informed consent documents to satisfy the HSRRB. Several months (from December 2006 to July 2007) were spent dealing with Dr. Inese Beitins who was subsequently relieved of her duties because of her actions on ours, as well as other, protocols. We then communicated with Amanda Ziehm and finally received approval from the HSRRB in January 2008.

We also spent several months satisfying the FDA's and the University of Iowa IRB's requirements. We were unable to respond to their recommendations until we obtained preliminary approval from the HSRRB, but this became a very tenuous situation in that the HSRRB would not provide final approval until we received FDA and IRB approvals. On the other hand, we could not obtain approvals from the latter agencies until we had "final" protocols and informed consent documents that satisfied the HSRRB's concerns. Thus, final approvals from all regulatory committees and agencies were obtained between October 2007 and January 2008.

The final hurdle was to satisfy the University of Iowa Health Care (UIHC) Pharmaceuticals and Therapeutics Committee that the Ad/PSA was stable and sterile. Several weeks were spent having the appropriate tests completed. The results demonstrated that the activity of the vaccine had not diminished during storage and that the product remained sterile, testing negative for aerobic and anaerobic bacteria and fungi.

Finally, on February 8, 2008 the clinical trial team began meeting to screen patients for eligibility into the trial. We have been treating patients since then and continue to meet to evaluate current patients and determine the eligibility of new patients.

We have treated four patients as of the submission of this annual report. They are:

Patient ID	Protocol	Arm	Discussion
APIIAHN-01	1	A	Hormone naïve patient has received the first vaccinations.
APIIAADT-01	1	B	This patient received androgen deprivation therapy and his first vaccination 14 days later.
APIIB-01	2	---	This patient received his first vaccination.
APIIAADT-02	1	B	The patient has begun androgen deprivation therapy and will receive the first vaccination on June 9.

Other patients are being screened for eligibility and a letter to referring urologists, medical oncologists, and radiation oncologists in the state of Iowa and the border areas of Illinois, Wisconsin, Minnesota, Missouri, and Nebraska.

To date the only adverse event, a grade 1, was a headache during the day following vaccination. All laboratory tests have been normal. The sera from the patients at their initial and return visits are being stored at -80 C. Lymphocytes, isolated from the peripheral blood of the patients, were stored in liquid nitrogen for future immunologic assays to be run as soon as all of the samples from the first year are collected for each patient.

KEY RESEARCH ACCOMPLISHMENTS:

Because we have only begun to treat patients there are no key research accomplishments at this time.

REPORTABLE OUTCOMES:

Similarly, there are no reportable outcomes at this time.

CONCLUSION:

After many months required to obtain approvals from the DOD's HSRRB, the FDA, and the University of Iowa IRB, we have begun accruing and treating patients in both protocols of the trial. There have not been any serious adverse events to date.

REFERENCES: None